

REMARKS

The Applicant now responds to the Advisory Action of November 16, 2005 by filing a Request for Continued Examination and this amendment. Claims 1-18, 21, 28-35, and 41-45 had been pending. In this paper, Applicant cancels composition claims 1-18 and claims 44-45 without disclaimer or prejudice to their introduction in another application. No other amendments are made, and no new matter is added to the claims. With this amendment, method claims 21, 28-35, and 41-43 are pending for Examination.

Deletion of Dr. Husband as an Inventor under 37 C.F.R. § 1.48(b)

This Amendment cancels the pending composition claims, leaving the method of treatment claims pending. Accordingly, Applicant seeks to amend inventorship by deleting Dr. Husband as an inventor under 37 C.F.R. § 1.48(b) because Dr. Kelly is the sole inventor of the method of treatment claims. A Request To Delete Originally Named Inventor Under 37 C.F.R. 1.48(b), as suggested by the Examiner, is filed concurrently with this response. This Request, together with Applicant's Rule 132 Declaration received December 13, 2004, establishes that U.S. Patent No. 6,340,703 is not the invention "of another." Accordingly, Applicant respectfully requests removal of this patent as prior art.

§ 103(a) Rejection of Claims 21, 28-35, and 41-43

The Office notes that "even upon removal of the Kelly patent, the claims rejection under 35 USC 103(a) would remain for reasons already of record." Advisory Action at 2. The Office then refers to Office Actions mailed April 13, 2005, and June 17, 2004, for maintenance of the 103 rejection of the claims for obviousness over Kelly WO 93/23069 (Kelly '069) in view of Empie et al. 6,261,565 B1 ("Empie") and Kelly 6,340,703 (Kelly '703).

In the June 17, 2004 Office Action, the Office states that Kelly '069 discloses compositions enriched with phyto-estrogens selected from genistein, daidzein, formononetin and biochanin A for promoting health in cases of cancer, premenstrual syndrome, menopause or hypercholesterolemia. The Office also states that Kelly '069's preferred ratio for genistein and/or biochanin A to daidzein and/or formononetin is 1:2 to 2:1 and that the compositions may be used to lower LDL thus leading to a reduced risk of developing atherosclerosis. Finally, the Office states that Kelly '069 does not specifically disclose using the compositions for treating osteoporosis or cardiovascular disease or vascular diseases or bone fractures.

The Office refers to Empie as disclosing compositions prepared by extracting phytochemicals from soy or red clover, wherein the resulting composition comprises isoflavones consisting predominantly of genistein and/or biochanin A and/or formononetin with a ratio of genistein to daidzein from 100:1 to 1:100. The Office states Empie additionally discloses that isoflavones are known to be useful in treating osteoporosis, vascular effects, and cardiovascular diseases, including heart disease.

The Office also refers to Kelly '703 as disclosing a method of treating osteoporosis by administering to a patient in need thereof a composition containing an effective amount (10:1 to 1:10) of formononetin and daidzein.

The Office concludes that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods and compositions of Kelly '069 for use in treating osteoporosis, vascular disorders or cardiovascular disorders because in view of Empie's and Kelly's '703 disclosure, one of ordinary skill in the art would reasonably expect the substantially similar isoflavone containing compositions of Kelly to be effective in treating such disorders." The Office also concludes the claims drawn to treating or preventing bone fracture

would have been obvious because one of ordinary skill in the art would reasonably expect the treatment of osteoporosis to reduce the likelihood of bone fractures.

The Office also states that it would have been obvious to one of ordinary skill in the art to modify the compositions of Kelly and Empie with additional calcium to help treat patients suffering from osteoporosis and bone fractures. Similarly, the Office states it would have been obvious to one of ordinary skill in the art to choose from a variety of known vitamins such that the overall composition is nutritionally balanced.

Finally, the Office states that “since Kelly ‘069 and ‘703 and Empie have established that the therapeutic efficacy of the isoflavones is dependent upon their ratio amounts, it would have been obvious to one of ordinary skill in the art to further modify the methods and compositions of Kelly and Empie such that the isoflavones are present in a ratio that is effective to optimize their therapeutic activity.”

Modified versions of the same assertions were set forth by the Office in the April 13, 2005 Office Action.

Applicant respectfully traverses because the Office has not set forth a *prima facie* case of obviousness. “To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference . . . must teach or suggest all claim limitations.” M.P.E.P. § 2143 at page 2100-135.

Applicant notes that the Kelly patent, U.S. Patent No. 6,340,703 cannot be applied as prior art against the invention because it has been removed as such by a combination

of the Rule 132 Declaration filed December 24, 2004 and the present Request to Delete an Originally Named Inventor. Therefore, no discussion of Kelly '703 is necessary, as it can no longer be applied as prior art.

As noted in Applicant's December 13, 2004 Amendment and Response to the June 17, 2004 Office Action, neither Kelly '069 nor Empie teaches or suggests "high proportions of formononetin." Indeed, both references expressly teach away from this concept.

Beginning with the Kelly '069 publication, it teaches a composition of any or all four isoflavones. The "Disclosure of Invention" at page 8 recites a supplement "specifically enriched for isoflavones selected from genistein, daidzein, formononetin, and biochanin A." It later states that the ratio of genistein (and/or its derivative biochanin A) to daidzein (and/or its derivative formononetin) is between 1:2 to 2:1. This ratio provides no teaching or suggestion about high proportions of formononetin.

Moreover, the Kelly '069 specification makes clear that it does not matter whether or not formononetin or its demethylated form, daidzein, is present, as follows:

It is thought that because the methyl forms (biochanin A and formononetin) ultimately are largely demethylated to their principles, genistein and daidzein, with improved biological efficacy, then it is *unimportant whether the isoflavones are present in the claimed product in methylated or demethylated forms.*

Specification, page 10, paragraph 2 (emphasis added). And still later the specification teaches that "it is prudent that both [isoflavone groups (being genistein and daidzein)] be present in the claimed product in *approximately equal proportions.*" *Id.* paragraph 3 (emphasis added).

Finally, as the Office acknowledged, the Kelly '069 publication does not disclose treating osteoporosis or bone fractures. Thus, it teaches away from "high proportions of formononetin" and is completely silent on the use of any isoflavone compositions for bone maladies.

Empie, the '565 patent, similarly teaches away from "high proportions of formononetin." Its background section concludes with the express proposition that "a need exists for an improved composition consisting substantially of isoflavones, lignans, saponogenins, saponins, and/or phenolic acids which will produce improved results *over any of these taken alone.*" Col. 3, lines 31-34 (emphasis added). Correspondingly, the Detailed Description begins by teaching that "the improved composition is obtained by fractionating a plant source high in isoflavones, lignans, and other phytochemicals..." col. 4, lines 16-18, and then later provides proportions for these mixtures, as follows:

The resulting composition is expected to comprise in a preferred from [sic]: between 5% and 95% isoflavones, between 0% and 70% lignans, and between 2% and 70% saponins and sapogenins.

Col. 4, lines 44-47.

The paragraph does discuss a ratio of the derivatives of genistein (and/or its precursor biochanin) to derivatives of daidzein (and/or its precursor formononetin) of from 100:1 to 1:100, but that range merely covers the entire spectrum. And none of the isoflavone-based compositions made in Examples 1-4 indicate the amounts of the specific isoflavones. The separate solutions in Example 5 were made merely to test solubility and do not even include one based on formononetin.

Finally, while Example 1 does mention osteoporosis, it does not even indicate whether the isoflavones are responsible for the beneficial results. It concludes that "isoflavones *or lignans* can alleviate menopausal-related symptoms such as hot flashes and osteoporosis...." Col. 7, lines 4-5.

Thus, Empie expressly teaches the value of mixtures of these various phytochemicals, and specifically teaches mixtures of isoflavones. Because both teachings are diametrically opposed to "high proportions of formononetin," Empie teaches away from the claimed invention.

As is well established, the Office cannot set forth a *prima facie* case of obviousness based upon references that teach away from the claimed invention. Manual of Patent Examining Procedure § 2145 at 2100-168 - 2100-169; *In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986). Accordingly, Applicant respectfully requests the withdrawal of the obviousness rejection under 35 U.S.C. § 103(a).

CONCLUSION

With the entry of this Amendment, claims 21, 28-35, and 41-43 are pending. Applicant earnestly and respectfully requests the Office to reconsider its assertion of *prima facie* obviousness and to allow the pending amended claims. Should this paper not result in a Notice of Allowance, Applicant respectfully requests that the Examiner contact the undersigned at 650-849-6611 to arrange for an interview.

If there is any further fee due in connection with the filing of this Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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